An interesting case of tall cell carcinoma of the breast with reverse polarity

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Abstract

We report a rare case of tall cell carcinoma of the breast with reverse polarity (TCCRP) in a woman who presented with a newly found breast lump. TCCRP is a rare subtype of papillary breast carcinoma that has similar appearance to tall cell papillary thyroid carcinoma. TCCRP is a rare tumour with unclear pathophysiology but is most frequently seen in postmenopausal women. It typically presents with triple negative phenotype. Diagnosing TCCRP can present diagnostic challenges due to its rarity and resemblance to other benign and malignant lesions of the breast with worse prognosis.

Keywords Breast carcinoma; breast pathology; papillary carcinoma of breast; reverse polarity; tall cell carcinoma; tall cell variant papillary thyroid carcinoma

Case report

A postmenopausal woman presented to her GP on discovery of a new unilateral breast lump with no other associated symptoms. She was otherwise fit and well with no past medical history of note, nor family history and had attended previous breast screening. Examination was suspicious for breast cancer with a nodular lump in her lower outer quadrant. She was referred for review in breast clinic, where examination found a vague nodular area with no defined border with dense tissue and was scored as P4. Ultrasound investigation showed a 17 mm x 15 mm hypoechoic irregular unilateral suspicious mass corresponding to the patient's palpable lump, with benign looking nodular opacities and microcalcification. The radiological score was R5. Ultrasound guided core biopsies were taken with no complications, yielding 4 tissue cores.

On microscopy, these cores show circumscribed nests of epithelial cells that sit within a dense fibrous stroma admixed with fat. Most of the nests show fibrovascular cores imparting a solid papillary pattern (Figure 1). Foamy histiocytes are present within the fibrovascular cores. The tumour cells are tall and columnar, with nuclei present at the apical aspects (Figure 2). Consequently, the favoured diagnosis for biopsy of this breast lesion is a tall cell carcinoma with reverse polarity (TCCRP) and a B5b coding was given for invasive carcinoma. Immunohistochemistry was performed for ER (Figure 3) and PR (Figure 4) tumour cell expression, demonstrating low focal positivity of both receptors at 1−10% each. Testing for HER2 overexpression was negative. TTF-1 and Thyroglobulin IHC were also negative. CK5 staining was mostly positive which is characteristic for TCCRP and is a reflection of the basal phenotype. Further staining was not performed as morphology was characteristic of TCCRP.

The patient was discussed in Breast MDT and referred for a wide local excision and sentinel lymph node biopsy, with results awaited. Further molecular testing is pending to identify if there are any mutations in PIK3CA or IDH in this lesion.

Discussion

Tall cell carcinoma with reverse polarity (TCCRP) was first described in 2003 by Eusebi as a variant of papillary breast carcinoma, comprising abundantly eosinophilic columnar and cuboidal tall tumour cells arranged in nests, papillae and follicle-like structures.[1] Nuclear features appear bland and nuclei are apically orientated instead of at the basal pole, therefore giving the cellular appearance of reverse nuclear polarity. Moreover, foamy histiocytes can aggregate in fibrovascular cores. Macroscopically, TCCRP may present as a well circumscribed, firm, white-grey mass with median size around 1.5 cm, but can be cystic with colloid resembling thyroid tissue.[2] Strong similarities have been drawn with the tall cell variant papillary thyroid carcinoma due to histological features resembling thyroid tumour, so can be misinterpreted on biopsy.[3]

TCCRP is considered to be an infrequent variant with only around 80 cases published and has recently been included as a separate subgroup of rare tumours in the WHO Blue Book Classification of Breast Tumours (5th edition).[4] TCCRP is most commonly seen in postmenopausal women, with median age 64 years, presenting with a palpable breast lump.[2]

Immunohistochemistry is an important distinguisher between both benign and malignant differential diagnoses which would be

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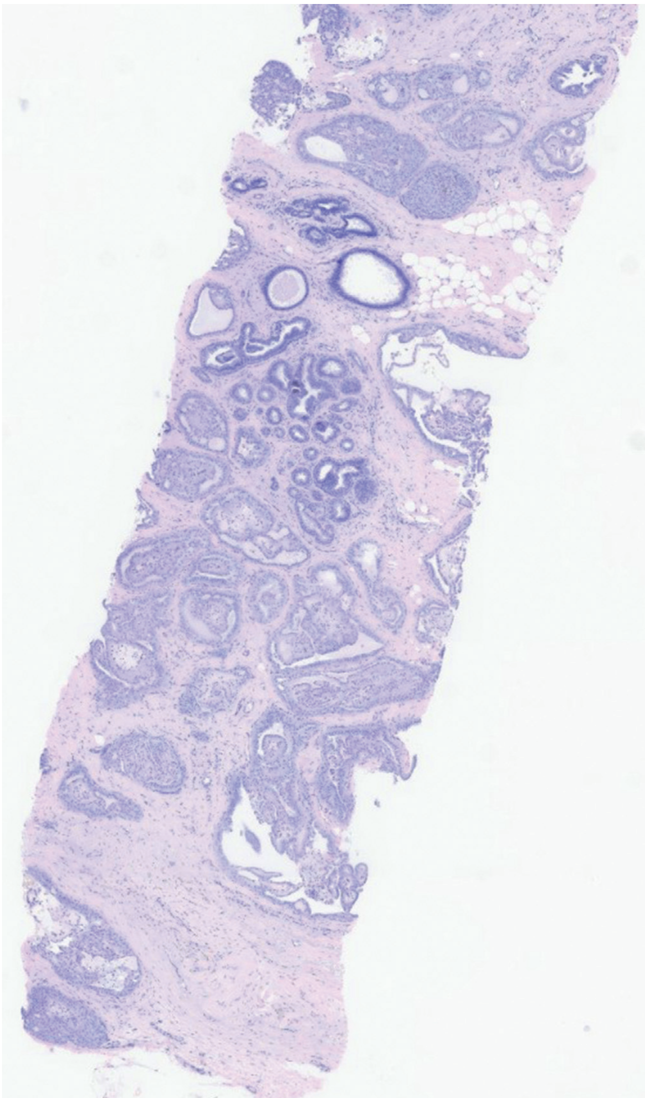

Figure 1 Circumscribed nests of epithelial cells in fibrous stroma.

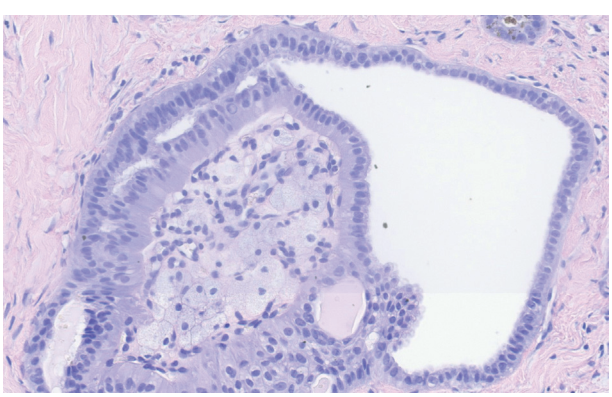

Figure 2 Tall and columnar tumour cells with apical nuclei consistent with tall cell carcinoma with reverse polarity.

managed in contrasting ways.[3] In TCCRP, tumours are typically triple negative for hormone receptors ER/PR/HER2, or weak positive in the 1–10% range, as seen in this case, with overall low malignant potential and good prognosis.[5] Consequently,

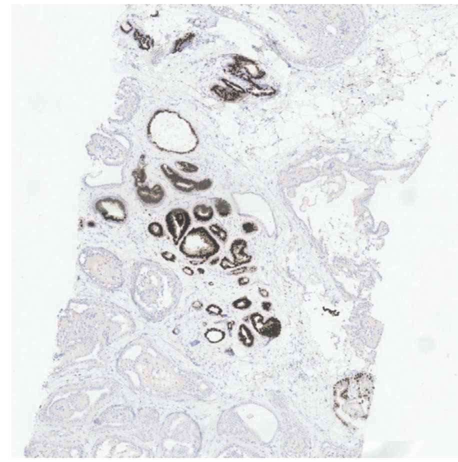

Figure 3 ER focal positivity (1–10%).

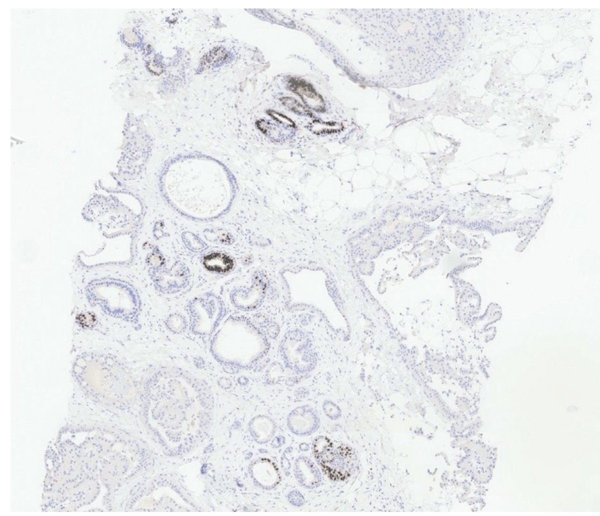

Figure 4 PR focal positivity (1–10%).

surgical excision is the mainstay treatment[2] and was done in this case as a wide local excision.

TCCRP can pose diagnostic challenges, underscoring the significance of distinguishing it from other potentially more aggressive conditions which share certain histological features. For example, ruling out metastatic thyroid carcinoma.[1] Tall cell is the most common variant of papillary thyroid carcinoma and warrants careful attention due to its aggressive form, requiring more intensive treatment and increased frequency surveillance due to higher recurrence. Microscopically, it comprises well-formed papillae with a tall columnar cell layer and is most commonly unencapsulated and infiltrative. Most of these tumours harbour BRAF V600E mutations, distinct from TCCRP which predominantly exhibits IDH2 R172 hotspot mutations upon molecular testing.[6] Other significant differential diagnoses to consider include solid papillary carcinoma, encapsulated papillary carcinoma, and intraductal papilloma with usual ductal hyperplasia.[3] A comparative overview of the immunoprofile distinctions between these is provided in Table 1 for further reference.

Comparative typical immunoprofile and molecular mutations for tall cell carcinoma with reverse polarity and differential diagnoses[1,3]

Tall cell carcinoma with reverse polarity	Metastatic thyroid carcinoma	Solid papillary carcinoma	Encapsulated papillary carcinoma	Intraductal papilloma with usual ductal hyperplasia
ER−	TTF-1+	ER+ (strong)	CK5/6−	CK5/6+
PR−	Thyroglobulin+	Variable CK5/6	ER+	SMMHC+
HER2−	BRAF and RET/PTC mutations			P63+
IDH2 R172 hotspot mutation				
PIK3CA hotspot mutation				

Table 1

Conclusion

In conclusion, we present an interesting case of the rare breast tumour subtype, tall cell carcinoma with reverse polarity. This has a distinct histological appearance and should be considered as a differential diagnosis in postmenopausal women with a breast lesion morphologically resembling tall cell papillary thyroid carcinoma. In general, triple negative breast cancers usually have a worse prognosis and different treatment pathway, therefore it is important to recognise TCCRP as a more indolent and less aggressively behaved subtype. Additional investigations should be considered, such as genetic testing for distinct hotspot mutations. ◆

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Practice points

- Tall cell carcinoma with reverse polarity (TCCRP) is a rare condition most seen in postmenopausal women
- IDH2 R172 hotspot mutation is the most common molecular mutation in TCCRP
- TCCRP tumours are usually triple negative (ER/PR/HER2) or have low focal positivity
- Although these are triple negative tumours, the prognosis is typically good
- It is important to recognise histological mimics from other sites, such as the more aggressive tall cell variant papillary thyroid carcinoma, papillary lesions in the breast and other benign conditions. This can help avoid unnecessary clinical and radiological investigations

Self-assessment multiple choice questions

1. Which of the following are NOT true of tall cell carcinoma with reverse polarity?

a. It histologically resembles tall cell variant of papillary thyroid carcinoma
b. It most commonly occurs in postmenopausal women
c. It has nuclei abnormally present at the basal aspect of epithelial cells
d. It is usually treated by surgical excision
e. It is arranged in solid circumscribed nodules of columnar epithelial cells

Correct answer: c

2. Which immunoprofile best matches that of a tall cell carcinoma with reverse polarity?

a. CK5/6 negative, ER positive
b. Strong ER positive, variable CK5/6
c. CK5/6, SMM and p63 positive
d. Strong ER, PR and HER2 positive
e. ER, PR and HER2 negative

Correct answer: e

3. Which is the most common genetic mutation in tall cell carcinoma with reverse polarity?

a. IDH2 R172 hotspot mutation
b. BRAF V600E mutation
c. RET mutation
d. PTC mutation
e. IDH1 mutation

Correct answer: a

